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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/677,701	10/02/2003	Victor V. Levenson	NWESTERN-08390	9778

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EXAMINER	
GOLDBERG, JEANINE ANNE	
ART UNIT	PAPER NUMBER
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/677,701	LEVENSON ET AL.	
	Examiner	Art Unit	
	Jeanine A. Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 21-32* is/are pending in the application.

4a) Of the above claim(s) *29 and 30* is/are withdrawn from consideration.

5)☒ Claim(s) *3-14 and 32* is/are allowed.

6)☒ Claim(s) *1,2,21-25 and 31* is/are rejected.

7)☒ Claim(s) *26-28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed October 18, 2006. Currently, claims 1-14, 21-32 are pending.

2. Claims 29-30 are withdrawn from consideration as drawn to non-elected subject matter.

3. Any rejections not re-iterated herein are hereby withdrawn.

A) The 103 rejection on Claim 3 which was previously directed to Yan et al. in view of Ferguson and Herman and Bovenzi and Du and Paz and Worm has been withdrawn in view of the amendments to the claims to require an association with breast cancer. The prior art does not appear to teach detecting DAPK to characterize breast cancer. Thus, the ordinary artisan would not have been motivated to analyzed DAPK with the other known breast cancer associated genes.

Election/Restrictions

4. In view of the amendments to the claims to require a combination of all 8 genes in Claim 3, the restriction requirement to a particular combination of genes has been withdrawn.

Newly Added Claims 29-30 are drawn to combinations of promoters not previously elected. In the event that the generic claim becomes allowable, the combinations comprising at least 5 or 40 genes would be rejoined.

Priority

5. This application claims priority to provisional 60/415,628, filed October 2, 2002.

Drawings

6. The drawings are acceptable.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-2, 21, 23-24, 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kusui et al. (Biochemical and Biophysical Research Communications, Vol. 289, pages 681-686, 2001) in view of Yan et al. (Clinical Cancer Research, Vol. 6, pages 1432-1438, April 2000).

Kusui teaches analysis of DNA methylation of the human oxytocin receptor gene promoter that regulated tissue specific gene suppression. Kusui teaches digesting genomic DNA with methylation sensitive restriction enzyme HpaII and amplifying the promoter with gene specific primers. Kusui specifically teaches peripheral blood was obtained from humans. Genomic DNA was extracted from tissues and digested with BamHI and HpaII which are both methylation sensitive enzymes. The digested DNA was analyzed by PCR using primers specific for the OTR gene (page 683, col. 1). Kusui specifically teaches that after the complete digestion of the genomic DNA, fragments were amplified with PCR (page 684, col. 2)(limitations of Claim 31).

Kusui does not specifically teach analysis of a plurality of promoters.

However, Yan et al. teaches Cpg Island arrays for deciphering epigenetic signatures of breast cancer. Yan teaches an array based method for differential methylation hybridization (DMH) which allows for genome-wide screening of Cpg island hypermethlation. Yan specifically teaches obtaining patient samples from female patients undergoing mastectomies to isolate high molecular weight DNA (limitations of Claim 21, 24). Yan further teaches analyzing genomic DNA that was digested and amplified (page 1433, col.1). Yan teaches performing array hybridization on nylon membranes (page 1433, col. 2). Yan teaches normal and tumor amplicons were

analyzed (limitations of Claim 2). As seen in Figure 1, the results of DMH are illustrated. CpG island tags were arrayed for secondary DMH screening in the patient group. Yan teaches the array based method allows semiquantification of the methylation differences, hybridization signal intensity. Moreover, Yan teaches the benefits of DMH such that high-throughput microarray based assays allow for detection of many CpG island hypermethylation at the whole genome level.

Therefore, it would have been prima facie obvious at the time the invention was made to have performed the method of Kusui to detect methylation in promoter regions of known genes and improved the detection method using the array based analysis of Yan. Kusui specifically teaches obtaining amplicons from methylated nucleic acids. The ordinary artisan would have been motivated to have generated a high-throughput analysis of the amplicons on an array, as taught by Yan to obtain the expected benefits of analysis of numerous nucleic acids simultaneously and allow detection at the whole genome level. Thus, analyzing the amplicons generated by Kusui on an array taught by Yan would have been obvious at the time the invention was made for the specific benefits of high-throughput taught by Yan.

9. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kusui et al. (Biochemical and Biophysical Research Communications, Vol. 289, pages 681-686, 2001) in view of Yan et al. (Clinical Cancer Research, Vol. 6, pages 1432-1438, April 2000) as applied to Claims 1-2, 21, 23-24, 31 above and further in view of Huang (US Pat. 6,605,432, August 12, 2003).

Neither Kusui, nor Yan, specifically teach using the Hin6I methylation sensitive enzyme for digesting.

However, Huang teaches analysis of high throughput methods for detecting DNA methylation. Huang teaches after amplification, methylation-sensitive sites of the amplified products are preferably identified by digestion with a methylation-sensitive restriction enzyme. Examples of such methylation-sensitive enzymes are BstU I, SmaI, SacII, EagI, MspI, HpaII, HhaI and BssHII which digest non-methylated CpG dinucleotide regions (limitations of Claim 14). Positive CpG dinucleotide nucleic acid fragments containing the methylation-sensitive sites are used for DMH analysis.

Therefore it would have been prima facie obvious to the skilled artisan at the time the invention was made to modify the method of Kusui, and Yan, to digest with Hin6I, an equivalent methylation sensitive enzyme. Kusui teaches digesting with HpaII. Huang teaches that BstUI and HhaI (also known as Hin6I) are methylation sensitive enzymes for digesting and analysis of methylation patterns.

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Central Fax Number for official correspondence is (571) 273-8300.

J. Goldberg

Jeanine Goldberg
Primary Examiner
January 5, 2007